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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,835	07/05/2000	HANS PROPPERT	HARMSEN002	8966

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EXAMINER
MARX, IRENE

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,835	PROPPERT, HANS	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

The application should be reviewed for errors. Error occurs for example at page 9 of the specification in the use of "..." for the CFU/ml amount. No new matter may be added.

DETAILED ACTION

The amendment filed 5/6/03 is acknowledged. Claims 2-21 are being considered on the merits.

Claims 2-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 3, 4 and 17 are vague, indefinite and confusing in requiring the administration of a viable strain without indication of the mode of administration. Since oral administration appears implied by the disclosure, claims 5, 7, 9 and 18 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, if oral administration is intended. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 102

Claims 2-10, and 17-18 remain/are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hockertz [AT] or Lodinova-Zadnikova et al. [AR] or under 35 U.S.C. 102 (a) as being clearly anticipated by DE 196 37 936 [AL] for the reasons as stated in the last Office action and the further reasons below.

The claims are directed to preventing or treating diarrhea in a mammal, including diarrhea mediated by pathogenic fungi, comprising administering viable *E. coli* DSM 6601.

Response to Arguments

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

In response to applicants' arguments that Hockertz administers the material for a different purpose, it is noted that the same viable strain of *E. coli* is provided to the same subject as in the instant claims. Moreover, the contention that the causal agents and the *E. coli* DSM 6601 suspension are in direct contact in the invention is puzzling, since this is not part of the claim designated invention. Furthermore, the prophylactic method of Hockertz cannot be patentably distinguished over the prophylactic and treatment method of the instant invention. Clearly, once the viable *E. coli* DSM 6601 are orally administered, they will be effective throughout the body regardless of the intended target at the moment of administration to at least prevent diarrhea. In other words, the oral administration of viable *E. coli* DSM 6601 in a therapeutically effective amount inherently prevents and/or treats diarrhea in a mammal. Note also that it is recognized in the written disclosure that the strain acts by increasing the body's endogenous defense mechanisms by immuno-stimulation (Specification, page 6, paragraph 3).

With respect to the issue of whether patents to "second medical uses" are or are not approved at the PTO, it is noted that each application is examined on its own merits. In response Applicants' arguments regarding the clear patentability of hypothetical claims for the treatment of artherosclerosis over claims directed to the treatment of hypertension with an effective amount of aspirin, it is are noted that patentability of such claims would hinge upon the precise language of the claims as well as the disclosure in the specification as to whether the respective process claims do or do not read on the same process, including a process of administration of aspirin for headaches or other pain, in view of the biochemical pathways or mechanisms of action involved.. Whether a process claim is patentable or not depends not only on the claim preamble, but also on the body of the claim, including process steps and parameters

such as dosage, mode of administration, the nature of the patient to be treated and the biochemical pathways and mechanism of action of the compound or composition. If the steps, dosage, mode of administration, patient and/or biochemical pathways/mechanisms of action are reasonably expected to be substantially the same as in the prior art for the same compound or composition, the process is unlikely to be patentable, since it lacks novelty or would be obvious over the prior art.

Applicant is correct in that antibiotics that work against bacteria are not necessarily effective against fungi. However, this is not relevant to the claimed invention. There is no indication in the present record that the strain *E. coli* DSM 6601 produces a particularly effective antibiotic, but rather there is every indication that the strain acts by competitive exclusion upon colonization of the intestine and/or by stimulating the immune system. At least competitive exclusion is shown in the prior to be successful for strain *E. coli* DSM 6601 at least in Lodinova-Zadnikova et al. (See, e.g., page 225, col. 2), and which appears to be the basis of "prevention" as claimed at least to some extent. The issue of whether fungi were searched and/or found in the stools of the children treated is irrelevant to the process of the rejected claims (Response, page 8).

With respect to the German patent, it is noted that the present claims merely require the one step of administration of the strain for prevention and treatment. The bioadhesive properties of the strain assure colonization of the gut, which is all that is necessary for successful competitive exclusion of pathogens, including fungi, for example. Also, it is noted that the reference recognizes the benefits of the administration of the strain at Translation, page 12, paragraph 2, citing in particular effectiveness against recurring diarrhea.

In response to applicants doubts that the strain is still viable after administration in conjunction with nystatin, it is noted that nystatin is an antimycotic and would not reasonably be expect to affect the viability of *E. coli*.

It is also of interest to emphasize that the written disclosure acknowledges that the effectiveness of the strain *E. coli* DSM 6601 depends at least to some extent on competitive exclusion. In addition, it is stated that the strain acts by increasing the body's endogenous defense mechanisms by immuno-stimulation (Specification, page 6, paragraph 3).

Therefore the rejection is deemed proper and it is adhered to.

Claim Rejections - 35 USC § 103

Claims 2-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Hockertz [AT] taken with Lodinova-Zadnikova et al. [AR] and DE 196 37 936 [AL] .

Hockertz disclose the administration of DSM 6601 (Nissle 1917) to mice. This administration has prophylactic effects on fungi such as *Candida* which are due to immunostimulation (See, e.g., bridging paragraph between pages 795-796). Lodinova-Zadnikova *et al.* disclose the administration of DSM 6601 to humans (See, e.g., page 225). This administration has the effect of protecting mammals such as humans from diarrhea, which would include fungi-mediated diarrhea. In addition, DE 196 37 936 teaches the administration of DSM 6601 to treat intestinal infections with *Candida* infection (p. 12 of translation), which is the same microorganism treated in the instant written disclosure.

The references differ from the claimed in that the treatment of ruminants, and bovines in particular, is not disclosed. However, the instant written disclosure acknowledges that the process of immuno-stimulation disclosed by Hockertz and the adhesive properties for colonization disclosed by the German patent constitute the same mechanism of action for strain DSM 6601 as the effect of the strain recognized in the instant specification, i.e. that it acts not only by competitive exclusion, but also by increasing the body's endogenous defense mechanisms by immuno-stimulation (Specification, page 6, paragraph 3). Therefore, one of ordinary skill in the art would have reasonably expected the same effects of competitive exclusion and immuno-stimulation on any mammal including ruminants, such as bovines, and in particular to newborn calves, in view of the beneficial effects disclosed in the cited art of the administration of viable *E.* coli DSM 6601 to other mammals, including newborn humans as taught by Lodinova-Zadnikova *et al.* Since the process as claimed requires the administration of viable *E.* coli DSM 6601, and the prior art cited teaches the administration of identical viable *E.* coli DSM 6601 for the same purposes of competitive exclusion of harmful fungi such as *Candida* as well as protective immunostimulation, one of ordinary skill in the art would have reasonably expected at the time the claimed invention was made that upon administration of viable *E. coli* DSM 6601, the viable bacteria are effective throughout the body regardless of the intended target at the moment of administration.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of preventing and/or treating diarrhea, including fungal diarrhea, of Hockertz [AT], Lodinova-Zadnikova et al. [AR] and DE 196 37 936 [AL] by providing viable *E. coli* DSM 6601 in therapeutically effective amounts to ruminants such as bovines, for the expected economic benefit of maximizing the yield of agronomically valuable animals that are healthy and suitable for the production of meat or milk for human consumption.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (703) 308-2922. The examiner can normally be reached on Monday through Friday from 6:30 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The appropriate fax phone number for the organization where this application or proceeding is assigned is before final (703) 872-9306 and after final, (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service whose telephone number is (703) 308-0198 or the receptionist whose telephone number is (703) 308-1235.

Irene Marx
Primary Examiner
Art Unit 1651